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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,613	09/26/2003	Gerd Dannhardt	104035.269169	3699

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EXAMINER	
COPPINS, JANET L	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 10/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/672,613	DANNHARDT ET AL.	
	Examiner	Art Unit	
	Janet L. Coppins	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-7,12-15 and 21-30* is/are pending in the application.

4a) Of the above claim(s) *28-30* is/are withdrawn from consideration.

5)☒ Claim(s) *1-3, 5-7, 12-15, 22, 24-27* is/are allowed.

6)☒ Claim(s) *21 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3, 5-7, 12-15, and 21-30 are pending in the instant application.

Priority

1. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Germany on March 26, 2001. It is noted, however, that applicant has not filed a certified copy of the German application as required by 35 U.S.C. 119(b).

2. Applicant has also not provided a certified copy of the EP 2002/03264 PCT application of March 22, 2002.

3. Accordingly, Applicant cannot obtain benefit of foreign priority papers until the conditions of 35 U.S.C. 119(a-d) have been met.

Response to Amendment

4. Receipt is acknowledged of Applicants' Amendment and Response, filed July 7, 2005, which has been reviewed by the Examiner. Accordingly, claims 4, 9-11, 16, and 18-20 have been cancelled, and claims 1, 2, and 12-14 have been amended. New claims 24-30 have been added.

Election/Restrictions

5. Newly submitted claims 28-30, drawn to cosmetic compositions, are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Applicants originally elected claims 1-20, drawn to compounds and pharmaceutical compositions, classified in classes 548 and 514. The new claims are drawn solely to cosmetic compositions, classified in class 424, which were not included in the original search strategy.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 28-30 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

6. However, claims 21-23, drawn to methods of use, previously withdrawn from consideration, are now rejoined for examination on the merits since the product claims from which they depend appear to be allowable (see below).

Claim Rejections - 35 USC § 102

7. (a) Claims 1, 3, 19, and 20 previously rejected under 35 U.S.C. 102(b) as being anticipated by Niedballa et al, U.S. 4,355,039.

(b) Claims 1-3, 5, 7, and 20 previously rejected under 35 U.S.C. 102(b) as being anticipated by Mustafa, A. et al, Journal fuer Praktische Chemie.

(c) Claims 1-3, 6, and 20 previously rejected under 35 U.S.C. 102(b) as being anticipated by Gupta, G. D. et al, Indian Journal of Chemistry.

(d) Claims 1-3, 9-10, 14-15, 18, and 20 previously rejected under 35 U.S.C. 102(b) as being anticipated by Billheimer, Jeffrey et al, U.S. 5,318,984.

In view of Applicants' cancellations and amendatory changes, the Examiner withdraws the anticipation rejections to the above-mentioned claims.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 21 and 23 rejected under 35 U.S.C. 112, first paragraph, as not being enabled. The specification, while being enabling for compounds according to formula (I) for treating certain diseases that respond to the inhibition of cyclooxygenase, does not reasonably provide enablement for treating all of the diseases encompassed by the above claims. In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, applicants are claiming a method of treating any and all diseases that are connected with a disorder of the immune system.

The nature of the invention

The nature of the invention is of methods of treating immune system disorders/diseases, comprising administering a pharmaceutical composition comprising the instant claimed compound to a patient in need thereof. As stated, however, claims 21 and 23 recite that any or all immune system disorders/diseases are intended.

The state of the prior art

It is well recognized in the medical art that treatment of diseases or symptoms are not analogous terms. Furthermore, the diseases of claims 21 and 23 are not the same but different diseases. Treating diseases "which are connected with a disturbance of the immune system" encompasses thousands of diseases, including autoimmune and immunodeficiency diseases, for

example MS, AIDS/HIV, SCID, and CFS, of which there is no known cure. Such as all cancer patients require administering a cytotoxic/antitumor agent, on the other hand, treating autoimmune diseases employ the use of immunosupressants.

The predictability or lack thereof in the art

Treating autoimmune disorders/diseases, for example, involves administering immunosuppressive drugs, and the contemporary teaching in the art of immunosupressants is as follows (Ninham et al, WO 85/05031):

> " To date, immunosuppressive drugs that have been developed to manipulate the immune response, are usually compounds of complex structure that have been discovered by accident. Further, their mode of action is often unknown or very unpredictable and administration of the drugs can be accompanied by undesirable side-effects."

The immune response of a living organism is a complex, specific and interrelated process. It involves the overall coordination of all the lymphocytes, B-types, T-types, etc., their population, expression and interaction. The intertwined dependency and complexity in bio-feedback control relationships involves enormous biological pathways and physiological homeostasis.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

Furthermore, the instant claimed compounds have enzyme inhibitory activity, and enzyme inhibition is known to be stereospecific. Applicants are claiming a compound with a

large number of substituents having vast structural diversity, and have failed to provide any indication as to its stereoselective ability in regards to enzyme inhibition. Also, in the absence of a showing of correlation between all the diseases claimed as capable of being treated by the compound of claim 1 and the inhibition of cyclooxygenase, one of skill in the art is unable to fully predict possible results from the administration of the compound of claim 1.

The amount of direction or guidance present

The specification has enabled only the compounds according to formula (I) that selectively inhibit cyclooxygenase-1 and cyclooxygenase-2 enzymes. Treatment of the claimed distinct disorders/diseases are normally disease or symptom oriented, thus are highly individualized, i.e. treating the symptoms of eczema (itchy, inflamed skin) would not employ the same methods as treating the symptoms of rheumatoid arthritis (stiffness and joint pain). The efficacy of an individual compound against a specific disease or symptom needs to be specifically and individually supported by factual evidence. Such evidence has not been described or supported by the specification.

The presence or absence of working examples

The *in vitro* data provided in the disclosure for the inhibition of the cyclooxygenase pathway is insufficient evidence for methods of treating all diseases connected with an immune system disorder. In fact, the only disclosure in the specification at all is found in Tables 1-17, wherein the IC_{50} values of some exemplary compounds are provided. In view of the diversified multiple diseases as claimed, such a single universal disclosure fails to provide specific description in guiding one skilled in the art to pick and choose the specific compounds that would be useful for treating one or a specific group of pathological conditions. The standard of

35 USC 112, first paragraph rejections is that the application *itself* must inform, rather than direct, others to find out for themselves, please see *In re Garnder*, 166 USPQ 138.

The breadth of the claims

Applicants are claiming methods of treating a broad number of diseases that are unrelated. The allegation that the diseases claimed by the Applicants are all connected to the immune system is insufficient support that the claimed compounds have specific efficacy in current available form for treating all of the claimed diseases.

The quantity of experimentation needed

The quantity of experimentation needed is undue. One of ordinary skill in the art without direction, would be unable to treat each and every immune system disorder of claims 21 and 23, using the instant claimed compounds. One of skill in the art would need to determine what listed diseases would be benefited by the inhibition of the cyclooxygenase pathway and would furthermore then have to determine whether the claimed compounds would provide treatment of all of the disease by the inhibition of COX-1 or COX-2.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the claim 1 for the treatment of all immune system disorders. As a result,

necessitating one of skill to perform an exhaustive search for which claimed diseases can be treated by the compound of claim 1 in order to practice the claimed invention.

In order to overcome this rejection, the Examiner suggests incorporating "selected from the group consisting of" after "a disease that is connected with an immune system disorder" in claims 21 and 23 and including the diseases that Applicants are enabled for, namely some of the diseases described on page 14 of the specification.

Conclusion

10. Claims 1-3, 5-7, 12-15, and 21-30 are pending, claims 28-30 are currently withdrawn from consideration, claims 21 and 23 stand rejected, and claims 1-3, 5-7, 12-15, 22, and 24-27 appear to be allowable.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 571.273.8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Coppins
October 1, 2005

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